

REMARKS

The Request For Continued Examination (RCE) Transmittal, filed concurrently herewith in the above-identified application, is noted. This RCE Transmittal sets forth that the present amendments constitute the necessary Submission for the RCE Transmittal. In particular, note that the Amendment After Final Rejection submitted May 3, 2004, and the Supplemental Amendment After Final Rejection submitted May 26, 2004, are not to be entered as Submissions Under 37 CFR § 1.114; but, rather, the present amendments constitute such necessary Submission.

Note that the Amendment After Final Rejection submitted May 3, 2004, was refused entry in the Advisory Action mailed June 9, 2004, on the basis that the proposed amendments in this Amendment submitted May 3, 2004, raise new issues that would require further consideration and/or search, and that these proposed amendments are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

By the present amendments, the claims of the above-identified application are being amended consistent with amendments made in the aforementioned Amendment After Final Rejection filed May 3, 2004, and the Supplemental Amendment After Final Rejection filed May 26, 2004, and also to amend dependency of claim 5 to be dependent on claim 1, rather than on claim 11.

Specifically, claim 1 has been amended to recite that the method includes culturing a microorganism belonging to *Escherichia coli*, and to recite that this microorganism has resistance to 150 mg/l primaquine or the alkali metal salts thereof. In light of the amendments to claim 1, claims 11 and 12 have been

cancelled without prejudice or disclaimer. Moreover, as indicated previously, by the present amendments the dependency of claim 5 has been amended, such that claim 5 is now dependent on claim 1.

Applicants respectfully traverse the rejection of their claims under the first paragraph of 35 USC §112, as set forth on page 2 of the Office Action mailed November 3, 2003, particularly insofar as this rejection is applicable to the claims as presently amended. It is respectfully submitted that the claims as presently amended are clearly enabled by Applicants' original disclosure, particularly in view of the evidence presently of record (in particular, the Declaration Pursuant to 37 CFR §1.132 of T. Abe, submitted with the Amendment filed September 11, 2003).

Thus, the present claims recite a method for producing L-histidine, which includes, inter alia, culturing a microorganism belonging to *Escherichia coli*, this microorganism having an ability to produce L-histidine and having resistance to 150 mg/l primaquine or the alkali metal salts thereof, in a culture medium. It is respectfully submitted that Applicants' disclosure as a whole, especially in light of the knowledge of one of ordinary skill in the art and as can be seen in the aforementioned Declaration of T. Abe, provides sufficient guidance to one of ordinary skill in the art to practice the presently claimed method. In this regard, it is respectfully submitted, as acknowledged by the Examiner in indicating allowability of claim 5, that Applicants' original disclosure is enabling where the microorganism is *Escherichia coli* H-9341 (FERM BP-6674). As can be seen from Applicants' original disclosure (note, for example, Example 1 on pages 8 and 9 of Applicants' specification), Applicants show, through a specific embodiment with respect to mutant strain H-9340, an embodiment according to the present invention. General

guidelines for practicing the presently claimed method are set forth on page 8 of Applicants' specification; and while a specific example of the microorganism is set forth in the first full paragraph on page 7 of Applicants' specification, it is clear that other microorganisms, including mutant strains, can be used. Note, for example, the paragraph bridging pages 5 and 6, as well as the first and second full paragraphs on page 6 and the paragraph bridging pages 6 and 7, of Applicants' specification. Clearly, it would not constitute undue experimentation to determine materials having resistance to 150 mg/l primaquine or the alkali metal salts thereof, according to the process of the present invention. While some experimentation may be necessary, such experimentation would not be undue; and it is respectfully submitted that only undue experimentation causes a disclosure to be non-enabling. See In re Angstadt, 190 USPQ 214 (CCPA 1976). That is, it is respectfully submitted that one of ordinary skill in the art could culture a microorganism and determine its resistance to 150 mg/l primaquine or the alkali metal salts thereof; and, if resistant, and having an ability to produce L-histidine, would be enabling in connection with the presently claimed method. See In re Angstadt, supra.

It is respectfully submitted to be clear from the aforementioned Declaration of T. Abe, submitted September 11, 2003, that one of ordinary skill in the art could obtain a microorganism belonging to *Escherichia coli*, having an ability to produce L-histidine and having resistance to 150 mg/l primaquine or alkali metal salts thereof, without undue experimentation, according to the method described in Applicants' original disclosure. That is, the Declaration shows that three strains (H-9343 strain, No. 1 strain, and No. 2 strain), which are also resistant to 150 mg/l primaquine, that have excellent L-histidine productivity as great as or more than H-9341. It is

respectfully submitted that No. 1 strain and No. 2 strain are examples of microorganisms having an ability to produce L-histidine and having resistance to 150 mg/l primaquine or alkali metal salts thereof, which can be obtained according to the method described in the specification of the above-identified application, clearly supporting the conclusion that the original disclosure of the above-identified application would have been enabling as of the filing date of the above-identified application.

The contention by the Examiner in the paragraph bridging pages 2 and 3 of the Office Action mailed November 3, 2003, that from the data presented it cannot be readily ascertained that a selection with any other aminoquinoline would affect histidine production, since no clear correlation has been provided, is noted. However, the present claims recite resistance to primaquine or the alkali metal salts thereof, not "any other aminoquinoline" than primaquine. Moreover, it is respectfully submitted that Applicants' disclosure provides a simple test, clearly within the skill of the ordinary worker in the art, for determining materials having the ability to produce L-histidine and having the recited resistance. Clearly, the testing necessary does not constitute "undue" experimentation. Note In re Angstadt, supra.

The contention by the Examiner in the last full paragraph on page 2 of the Office Action mailed November 3, 2003, that strain H-9340 "is clearly required as indicated in the example 1 of the specification, to obtain the further strains touted in the declaration", is respectfully traversed. It is respectfully submitted that Applicants' disclosure as a whole, as originally filed, makes it clear to one of ordinary skill in the art that various microorganisms, including various strains from *Escherichia coli*, can be mutated in practicing the presently claimed method. Note, e.g., the paragraph

bridging pages 5 and 6 of Applicants' specification, disclosing that microorganisms used in the presently claimed method can be obtained by subjecting a microorganism to a conventional mutation treatment, and selecting colonies of the strain which grow more rapidly than that of the parent strain, or selecting colonies which are larger than that of the parent strain, among the resulting colonies being cultured. In view of all evidence of record, Applicants respectfully traverse the conclusion by the Examiner in the sentence bridging pages 2 and 3 of the Office Action mailed November 3, 2003, that from the data presented it cannot be readily ascertained that a selection with any other aminoquinoline would effect histidine production; to the contrary, it is respectfully submitted that all the evidence of record, including general guidance provided in Applicants' disclosure, establishes that the necessary enablement is provided for the presently claimed subject matter, including culturing a microorganism belonging to *Escherichia coli*, having an ability to produce L-histidine and having resistance to 150 mg/l primaquine or the alkali metal salts thereof.

The contention by the Examiner in the last full paragraph on page 2 of the Office Action mailed November 3, 2003, that there is no clear indication on the record that all restrictions on the availability to the public of the material deposited as FERM BP-6673 will be irrevocably removed upon the granting of a patent, is noted. It is hereby stated by the undersigned that any and all restrictions on the availability to the public of the material deposited as FERM BP-6673 will be irrevocably removed upon the granting of the patent. It is noted that the strain H-9340 was deposited under the Budapest Treaty as FERM BP-6673 as shown in the enclosed "RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT" (also submitted with the

Amendment After Final Rejection filed May 3, 2004), and it is confirmed by Applicants that all restrictions on the availability to the public of the material deposited as "FERM BP-6673" will be irrevocably removed upon the granting of a patent.

In view of the foregoing comments and present amendments, and also in view of the concurrently filed RCE Transmittal, withdrawal of finality of the Office Action mailed November 3, 2003, and entry of the present amendments; and reconsideration and allowance of all claims presently being considered on the merits in the above-identified application, are respectfully requested.

Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, or credit any overpayment of fees, to the deposit account of Antonelli, Terry, Stout & Kraus, LLP, Deposit Account No. 01-2135 (referencing case no. 506.39084X00).

Respectfully submitted,

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

[特許手続上の微生物の寄託の国際的承認に関するブダペスト条約]

下記国際寄託当局によって規則 7. 1 に従い
発行される。

原寄託についての受託証

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT

Issued pursuant to Rule 7. 1 by the INTERNATIONAL DEPOSITORY AUTHORITY identified at the bottom of this page.

氏名 (名称) 協和醸酵工業株式会社
寄託者 取締役社長 平田 正
あて名 東京都千代田区大手町一丁目6番1号

殿

1. 微生物の表示

(寄託者が付した識別のための表示)
Escherichia coli H-9340

(受託番号)
FERM BP- 6673

2. 科学的性質及び分類学上の位置

1 桁の微生物には、次の事項を記載した文書が添付されていた。

科学的性質
 分類学上の位置

3. 受領及び受託

本国際寄託当局は、平成 11 年 3 月 9 日 (原寄託日) に受領した1 桁の微生物を受託する。

4. 移管請求の受領

本国際寄託当局は、 年 月 日 (原寄託日) に 1 桁の微生物を受領した。
そして、 年 月 日 に原寄託よりブダペスト条約に基づく寄託への移管請求を受領した。

5. 国際寄託当局

通商産業省工業技術院生命工学工業技術研究所

名 称： National Institute of Bioscience and Human-Technology
Agenzia Nazionale per la Biologia e la Tecnologia
Japan Agency for
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平成 11 年 (1999) 3 月 9 日